Docket No. 700212 20.0031

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	)	
	)	
KENISON, DALE C. et al.	)	Group Art Unit 1616
	)	
Application No.: 09/589,730	)	Examiner: Levy, Neil S.
	)	
Filing Date: June 8, 2000	)	
	)	
Title: GROWTH PROMOTING PHARMACEUTICAL IMPLANT	)	

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

DECLARATION BY WILLIAM G. ZOLLERS

1. I am one of the inventors of the subject matter described and claimed in the above-referenced application.

2. This Declaration is being presented by me in furtherance of the prosecution of the above-referenced application, and demonstrates that the claimed implant functions to improve average daily gain and feed conversion efficiency of food animals in addition to preventing implant site abscesses in food animals.

3. Three studies were performed to evaluate the efficacy of growth-promoting implants also containing a pellet of a supplemental agent, namely, tylosin tartrate, in feedlot cattle.

4. Sanitation procedures used during the studies include removing debris from contaminated ears with a serrated knife or wire brush. Wet ears were washed with clean water then with a disinfectant solution. Ears that were clean and dry were implanted without further preparation. Implanter needles were dipped in disinfectant solution after each animal and dipped again if contact was made with the animal prior to implanting. Physical debris was removed from needles as necessary using sponges soaked with disinfectant. All implant products were kept in water-proof containers until use.

5. Implant site evaluations were conducted by an experienced evaluator who was unaware of the study design or treatment designation. For evaluation, animals were removed from the pen and restrained individually in the feedyard animal handling facility. Implant sites were inspected visually and by palpation.

6. Study One was conducted at a commercial feedyard in Oklahoma and utilized 438 mixed-breed yearling steers with a mean initial body weight of 361 kg. Steers were obtained as a single group, sorted by body weight (BW) into two blocks of two pens each, and placed on feed.

Within each pen, steers received either: (1) a growth-promoting implant containing 24 mg estradiol and 120 mg trenbolone acetate; or (2) a growth-promoting implant containing 24 mg estradiol, 120 mg trenbolone acetate, and 29 mg tylosin tartrate. Steers were assigned to treatment on an every-other-head basis within each pen wherein the treatment assignment of the first steer in each pen was determined randomly. Cattle were weighed individually on the day of implant. Implant sites were evaluated 28 days post-implant. Pens were slaughtered 125 days (two heavy pens) or 141 days (two lighter pens) post-implant. Hot carcass weights (HCW) were collected immediately after evisceration. Individual animal average daily gains (ADG) were calculated using the equation: ADG = ((HCW/0.635) - initial BW)/days on feed. In this equation, 0.635 represents the mean dressing percentage of all animals on the study. The results are shown below in Table 1.

Table 1. Results from Study One

	Treatment 1	Treatment 2	P =
Head evaluated	219	219	
Normal implant	214	218	
Abscessed implant site	4	0	
Missing implant	1	1	
Initial body weight (kg)	360.9	360.2	>0.5
Gain (kg) at 126 or 141 days	236.3	241.2	0.08
ADG (kg) at 126 or 141 days	1.76	1.80	0.07
Hot carcass weight	379.7	382.7	0.08

As shown in Table 1, a low incidence of abscesses was observed. In addition, there were higher body weight gains (P=0.08), higher ADG (P=0.07) and greater HCW (P=0.08) in the group that received Treatment 2.

7. Study Two was conducted in a commercial research facility in Texas and involved 1475 mixed breed steers with 360 kg initial weight. On day one, steers were divided into five groups and allotted from within each group in cycles of not more than 10 head per pen into 15 experimental pens. Pens contained between 89 and 111 steers each. Each allotment group was equally represented by % in each pen. Experimental pens were located in five geographic blocks of three pens each. After allotting cattle to pens, pens were randomly assigned to three treatments (one pen per block for each treatment). Experimental treatments were:

Table 2. Experimental Treatment Descriptions.

	Initial Implant	Re-implant
Treatment One:	24 mg estradiol 120 mg trenbolone acetate	None
Treatment Two:	24 mg estradiol 120 mg trenbolone acetate 29 mg tylosin tartrate	None
Treatment Three:	8 mg estradiol 40 mg trenbolone acetate	8 mg estradiol 40 mg trenbolone acetate 29 mg tylosin tartrate

Treatment three wa s re-implanted on day 50 of the 126 day study. Cattle were weighed as pens initially and at the conclusion of the feeding period. Feed was weighed and recorded prior to delivery. Implant sites were inspected at harvest at the slaughter facility. Carcass data were recorded after a 24 hour chill. The results are shown below in Table 3.

Table 3. Results of Study Two.

	Treatment 1	Treatment 2	Treatment 3	Probability > F	
				T1 v. T2	T2 v. T3
Proper implant (%)	97.8	99.4	99.4	NA	NA
Improper (%)	2.2	0.6	0.6	0.03	1.00
Abscessed (%)	0.4	0.2	0.0	NA	NA
Pellets missing (%)	0.8	0.2	0.0	NA	NA
Implant missing (%)	0.6	0.2	0.2	NA	NA
ADG (kg)	1.69	1.71	1.69	0.06	0.11
Feed/gain	5.67	5.60	5.62	0.04	0.03
HCW (kg)	370.9	373.6	372.3	0.11	0.44

As shown in Table 3, steers implanted with Treatment 2 had fewer implant site defects (P=0.03) despite a low incidence (2.2%) of implant site defects in the Treatment 1 group. Groups which received Treatment Two or Treatment Three had similar incidences of implant site defects. ADG and F/G of pens that received Treatment 2 were improved compared to those that received Treatment 1 and the initial implant of Treatment 3. The re-implant step of Treatment 3 also resulted in further improvement in F/G (P=0.03).

8. Study Three was conducted at a commercial feedyard in Kansas and utilized 532 mixed-breed yearling steers with a mean initial body weight of 363 kg. Steers were obtained as a single group, sorted by body weight into two blocks of four pens each, and placed on feed. Within each pen, steers received either: (1) a growth-promoting implant containing 24 mg estradiol and 120 mg trenbolone acetate; or (2) a growth-promoting implant containing 24 mg estradiol, 120 mg trenbolone acetate, and 29 mg tylosin tartrate. Steers were assigned to treatment on an every-other-head basis within each pen with the treatment assignment of the first steer in each pen determined randomly. Pens were slaughtered 127 days (two pens), 147 days or 156 days post-implant as determined by the feedyard manager. Cattle were weighed individually on the day of implant. Implant sites were inspected at harvest at the slaughter facility. HCW were collected immediately after evisceration. Individual ADG were calculated using the equation: ADG = ((HCW/0.644 - initial BW)/days on feed. In this equation, 0.644 represents the mean dressing percentage of all animals in the study. The results are shown below in Table 4.

Table 4. Results of Study Three

	Treatment 1	Treatment 2	P =
Head evaluated	263	269	
Total implant site defects (%)	2.3	2.2	>0.5
Initial body weight (kg)	368.8	368.3	0.49
Gain (kg) at 139 days	220.3	224.4	0.10
ADG (kg) at 139 days	1.58	1.61	0.09
Hot carcass weight (kg)	379.4	381.8	0.14

As shown by Table 4, there was a tendency for higher ADG (P=0.09) in the group that received Treatment 2. Differences in body weight gain (P=0.10) and HCW (P=0.14) were also significant.

9. In ongoing field evaluations of implant sites in commercial feedyards using a growth-promoting implant containing tylosin tartrate, experienced personal have palpated 164,656 implant sites with the following results:

Table 5. Results of Field Evaluations of Implant Sites.

	Growth-promotant w/o tylosin tartrate	Growth-promotant with tylosin tartrate
Head evaluated	111,651	53,005
Abscessed (%)	2.49	0.59

These evaluations were conducted upon customer request and do not represent a designed comparison of products. Nonetheless, the abscess rate with growth promotant and tylosin tartrate is 76% lower than without tylosin tartrate.

10. As these studies demonstrate, an implant containing a growth-promotant in synergistic combination with tylosin tartrate results in better animal performance, feed efficiency, and fewer abscesses than with an implant containing growth-promotants alone. While these studies were conducted with estradiol, trenbolone acetate and tylosin tartrate, it is expected that studies conducted using other active and supplemental agents as described and claimed in the present application would synergistically combine to demonstrate similar results.

11. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements and the like are punishable by fine or imprisonment, or both, under §1001 if Title 18 of the United States Code, and such willful, false statements may jeopardize the validity of any patents issued from the patent application.

May 2, 2003
Date

William G. Zollers